RESPONSE TO AMENDMENT

The amendment filed 7/28/08 has been entered into the record. Claims 1, 3-5, 48, 50-53, 55-60 and 62-66 have been cancelled. Claims 2, 6-47, 49, 54, 61 and 67 are pending and are under examination, however claim 67 is not treated further on the merits because of improper multiple dependency (see claim objection below).

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Specification

The amendment to the specification to correct the brief description of drawings filed 7/28/08 has been entered into the record. Accordingly, the objection to the specification made in the office action mailed 2/8/08 is withdrawn.

Claim Objections/Rejections Withdrawn

The objection to claims 2,7,18,19,28,29,38,39,54 and 55 is withdrawn in view of the amendment to the claims.

The rejection of claims 2,6,7,8,14,15,16,19, 23, 24,25, 29,30,33,34,35,39,43,44 and 45 under 35 U.S.C. 101 is withdrawn in view of the amendment to the claims.

The rejection of claims 18-47 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn upon further consideration.

The rejection of claims 54,55, 60,61,66 and 67 under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendment to the claims and the cancellation of claims 55, 60 and 66.

The rejection of claims 2, 6-24, 26-34, 36-44, 46, 47, 54-55,60-61 and 66-67 under U.S.C. 112, second paragraph, is withdrawn in view of the amendment to the claims and in view of the cancellation of claims 55, 60 and 66.

The rejection of 55 and 60 under 35 U.S.C. 102(b) as being anticipated by Saito et al. Gen. Pharmac, Vol. 28, p. 675-680, 1997 is withdrawn in view of the cancellation of the claims.

The rejection of claims 55 and 60 under 35 U.S.C. 102(b) as being anticipated by Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 is withdrawn in view of the cancellation of the claims.

The rejection of claims 2, 6, 7, 9, 10, 14, 15, 54, 55, 60 and 61 under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 view of Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and 477 is

withdrawn upon further consideration and in view of the cancellation of the claims 55, 60

The rejection of claims 2, 6, 7, 8, 10,14,15, 54, 55,60 and 61 under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 in view of Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 is withdrawn in view of the cancellation of the claims.

The rejection of claims 11-12 under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and 477 as applied to claims 2, 6, 7, 9, 10, 14, 15, 54, 55, 60 and 61 in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 is withdrawn upon further consideration and in view of the cancellation of the claims 55, 60.

The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and p. 477 and Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 as applied to claims 2, 6, 7, 9-12 14,15, 54,55,60 and 61 further in view of Alakhov et al. US 5,840,319, 1998 is withdrawn upon further consideration and in view of the cancellation of the claims 55, 60.

The rejection of claims 11-12 under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 as applied to claims 2, 6, 7, 8, 10,14,15, 54, 55,60 and 61 above further in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 is withdrawn upon further consideration and in view of the cancellation of the claims 55, 60.

The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 as applied to claims 2, 6, 7, 8, 10-12,14,15, 54, 55,60 and 61 further in view of Alakhov et al. US 5,840,319, 1998 is withdrawn upon further consideration and in view of the cancellation of the claims 55, 60.

Rejections Maintained

1) The rejection of claims 25, 35 and 45 under 35 U.S.C. 112, second paragraph is maintained for reasons made of record in the previous Office action mailed 2/8/08.

As to claims 25, 35, and 45 the claim is confusing because how can an antibody with an IgG variable region produced by hybridoma h13-17 or produced by hybridoma 5-89-2 or produced by hybridoma a44-1 also be an antibody of class IgA. The instant specification teaches

that the monoclonal antibodies produced by these hybridomas are of the class IgG and not IgA (see p.31 table 1).

Applicants did not address this issue in the reply filed 7/28/08.

2) The rejection of claims 2, 6, 7, 9, 10, 14,15, 54 and 61 under 35 U.S.C. 102(b) as being anticipated by Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 is maintained for reasons made of record in the previous Office action mailed 2/8/08.

3) The rejection of claims 2, 6, 7, 8, 10,14,15, 54, and 61 under 35 U.S.C. 102(b) as being anticipated by Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 is maintained for reasons made of record in the previous Office action mailed 2/8/08.

Applicants argument against Saito et al and Abiko et al are addressed:

The claims are drawn to an antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Applicants argue that induction of phagocytosis is not a necessary ("inherent") property of any antibody, simply by virtue of its ability to bind a target; rather, it constitutes a separate and distinct characteristic of *some* antibodies, pursuant to Applicants' claimed invention. Applicants provide support for this by citing Christiaansen et al (The Journal of Immunology 1987, vol. 138, 2236-2243). Applicants argue that Christiaansen et al describes how the spatial orientation of an antibody bound to a target cell influences the efficiency of phagocytosis, by affecting the

efficiency of interaction between the antibody-target complex and receptors of the phagocytic cells. Applicants state that Christiaansen demonstrates that specific antibodies that bind to target cells will vary in their ability to interact with receptors on phagocytic leukocytes. Applicants state that Christiaansen et al teaches that

"Although monoclonal (mAb) can elicit potent ADCC by human K lymphocytes, different mAb even of the same antibody subclass Or even of the same target antigen specificity, vary considerably as to their efficiency in eliciting ADCC" and "...because *the target antigen per se does not determine the ADCC effectiveness of a mAb (e.g., see Fig. 1), it is proposed here that exact region on the target antigen (the epitope) to which this mAb binds orients the antibody relative to other structures on the target cell membrane in such a way as to either permit or prevent the necessary Fc-FcR interactions for triggering ADCC*'

Applicants' arguments are carefully considered but are not deemed persuasive. The instant arguments are not commensurate in scope with the claims. The basis of Applicants arguments i.e. Christiaansen et al is drawn to a teaching of antibody dependent cellular toxicity (ADCC) and not to a teaching of antibodies promoting neutrophilic phagocytosis which is called opsonophagocytosis. The mechanism of opsonophagocytosis promoted by antibodies is fundamentally different from ADCC. In opsonophagocytosis, IgG (IgA also) molecules bind to and coat antigenic particles and the bound IgG is recognized by IgG Fc receptors on leukocytes serving to enhance the efficiency of phagocytosis. Both high and low affinity IgG Fc receptors contribute to phagocytosis and the IgG subtypes that bind best to these receptors (IgG1 and

IgG3) are most efficient for promoting phagocytosis (Abbas et al Cellular and Molecular Immunology. Third Edition. W.B. Saunders Company, Philadelphia, Chapter 3 pages 55-58).

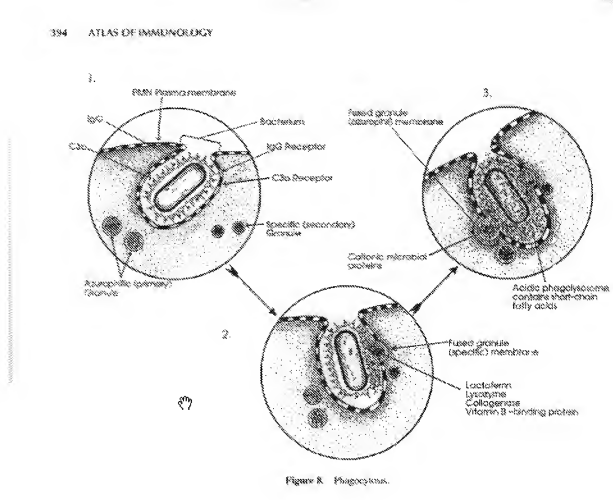

Figure 8 Phagocytosis.

See additional schematic of osponophagocytosis above (Atlas of Immunology, Julius Cruse, Robert Lewis, 1999, p. 391-394, CRC Press LLC, Boca Raton , FL, USA).

ADCC does not involve phagocytosis, instead in ADCC a leukocyte expresses low affinity Fc gamma receptors that recognize clustered immunoglobulin molecule prebound to target antigen

on the surface of a target cell and occupancy of the Fc gamma receptor serves to activate the leukocyte to synthesize and secrete cytokines such as tumor necrosis factor and interferon gamma as well as to discharge their granules. The released cytokines mediate inflammatory functions and the released granule proteins mediate lysis of the target cell (see Abbas et al cited above). Thus, the instant claims are drawn to antibody promotion of neutrophilic phagocytosis i.e. opsonophagocytosis and not to ADCC as argued by Applicants.

Furthermore, the instant claims do not distinguish the instantly claimed antibody by any structural characteristics that distinguish from Saito et al. Moreover, Saito et al teaches monoclonal antibodies to 40 kDa outer membrane protein (OMP of *P. gingivalis*) of the IgG1 isotype produced by several hybridomas including Pg-ompA2 which inhibited coaggregation of *P. gingivalis* (see table 1) and the reference also teaches on p. 679 column 1 paragraph before the discussion section, that IgG1 from Pg-ompA2 hybridoma opsonizes bacteria and has a high complement activating capacity. Abiko et al also teaches human monoclonal antibodies to 40 kDa outer membrane protein (OMP) of *P. gingivalis*. Thus, since antibodies of the subclass IgG are especially efficient in promoting phagocytosis by neutrophils (see Abbas cited above) and Saito teaches Pg-ompA2 IgG1 and also teaches that the antibody opsonizes bacteria and Abiko teaches IgG monoclonal antibodies; therefore the activity of Pg-ompA2 IgG1 of Saito et al or IgG of Abiko et al in promoting human neutrophilic phagocytosis is an inherent property of said antibody.

As to Applicants arguments that Saito et al or Abiko et al does not hint that the antibody that binds to 40 kDa outer membrane protein might suppress alveolar resorption and that this is Applicants discovery, is carefully considered but not persuasive. The recitation of suppressing

alveolar bone resorption is an intended use of the claimed antibody that binds to 40 kDa OMP. The claimed antibody must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim and in the instant case the claims do not recite structural characteristics of the instant antibody except that it binds to 40 kDa OMP. Thus, absent any other structural characteristics that distinguish from that of the prior art, then the instant antibody is capable of performing any of the intended uses including to suppress alveolar bone resorption due to *P. gingivalis*.

New Claim Objections/ Rejections Based on Amendment

Claims 11, 20, 30, 40 are objected to due to grammatical error. The claims recited the "the isolated antibody or the functional fragment of the antibody…which covalently or non-covalently conjugates to a therapeutic agent". Applicant may correct the grammar of the claims by reciting the "*the isolated antibody or the functional fragment of the antibody…which is covalently or non-covalently conjugated to a therapeutic agent*".

Claim 67 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

New Rejections

Claim Rejections - 35 USC § 112

Claims 2, 6-17, 54 and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated antibody an isolated antibody binding to 40-kDa outer membrane protein or a functional fragment thereof the antibody, which has (1) activity of inhibiting the coaggregation of *P. gingivalis* and (2) activity of promoting human neutrophilic phagocytosis. The claims are also drawn to an agent for suppressing alveolar bone resorption due to P. *gingivalis,* which contains an antibody binding to 40-KDa outer membrane protein or a functional fragment of the antibody as an active ingredient.

The claims are drawn to a genus of antibodies and functional antibody fragments that binds to a large and variant genus of 40 kDa outer membrane proteins. Said genus of antibodies is comprised of species that are variant in that they bind to any 40 kDa outer membrane protein. The specification does not teach which of these antibodies to any 40 kDa outer membrane protein has the activity of inhibiting the coaggregation of *P. gingivalis* and promoting human neutrophil phagocytosis except antibodies to the 40 kDa outer membrane protein of *P. gingivalis*. The specification does not teach the common epitope recognized by the antibodies to 40 kDa outer membrane protein of *P. gingivalis* that is shared with other 40 kDa outer membrane proteins so that one of skill in the art can envision other antibodies to other 40 kDa outer

membrane proteins possessing this shared epitope that can have the instant activities including suppressing alveolar bone resorption due to *P. gingivalis*. In order to satisfy the written description requirement, the application must reasonably convey to one skilled in the art that the Applicant was in possession of the claimed subject matter at the time the application was filed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). As of filing Applicants have not described which other 40 kDa outer membrane proteins share the same epitope recognized by the disclosed antibodies to the 40 kDa OMP and the disclosure of the antibodies to 40 kDa OMP of *P. gingivalis* is insufficient to describe the genus of antibodies to any 40 kDa outer membrane protein that have the recited activities. The written description requirement is separate and distinct from the enablement requirement (*Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir. 2004)) and adequate written description requires more than a mere reference to a potential method for identifying for example shared epitopes of other 40 kDa outer membrane proteins and making antibodies and screening for those which have the instantly recited activities. Amendment to the claims to indicate that the 40 kDa outer membrane protein is that of *P. gingivalis* would obviate this issue.

Claims 2, 6-26, 28-36, 38-46, 49, 54 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody of class IgG or IgA which bind to 40 kDa outer membrane protein of *P. gingivalis* wherein said antibody has the activity of inhibiting the coaggregation of *P. gingivalis* and activity of promoting human neutrophilic phagocytosis and for suppressing alveolar bone resorption due to *P. gingivalis* does

not reasonably provide enablement for antibodies of other classes such as IgM or IgD or IgE and does not provide enablement for functional fragments without the Fc portion of antibody binding to 40 kDa outer membrane protein of *P. gingivalis* which promote human neutrophilic phagocytosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to isolated antibody and functional fragments of said isolated antibody binding to 40 kDa outer membrane protein which have activity of promoting human neutrophilic phagocytosis and have activity of inhibiting the coaggregation of *P. gingivalis* and thus suppressing alveolar bone resorption due to *P. gingivalis*. As set forth above the claims (2, 6-17, 54 and 61) are broadly drawn to any antibody to any 40 kDa outer membrane protein as the claims as written do not specify the microorganism from which the 40 kDa outer membrane protein is obtained. The specification does not correlate any activity of an antibody to any 40 kDa OMP with therapeutic activity against *P. gingivalis* except antibody to 40 kDa OMP of *P. gingivalis*. It is unpredictable that an antibody to other 40 kDa OMP will have the same activity of the antibody to 40 kDa OMP of *P. gingivalis* and therefore more guidance and working example is needed to demonstrate the recited activities and whether such an antibody can suppress alveolar bone resorption due to *P. gingivalis*. Amendment to the claims to indicate that the 40 kDa OMP is of *P. gingivalis* will obviate this issue.

Also, the claims as written are broadly drawn to any immunoglobulin class of the instant antibody or functional fragments thereof that have activity of promoting human neutrophilic phagocytosis and have activity of inhibiting the coaggregation of *P. gingivalis*. However, the art

teaches that not all antibody subclasses are able to bind to neutrophils and promote phagocytosis of antibody bound bacteria. For example, IgM, IgD and IgE do not bind to phagocytes and IgE binds to mast cells and basophils (Lucas et al. Antibody Structure. Encyclopedia of Life Sciences 2001, John Wiley and Sons, Ltd. See p. 2 table 1). Thus, since the art teaches that IgM, IgD and IgE do not bind phagocytes then more guidance or working example is needed to contradict the art teachings that IgM, IgD and IgE antibodies to the instant antigen promote human neutrophil phagocytosis or suppress alveolar bone resorption by *P. gingivalis*. The specification is devoid of such data and one of skill in the art as of the time of filing would not have believed that IgM, IgD and IgE antibodies can promote human neutrophilic phagocytosis.

As to the activity of functional fragment of the instantly claimed isolated antibody for promoting human neutrophilic phagocytosis, the use of antibody fragments for promoting neutrophilic phagocytosis (opsonization) is unpredictable. The classic antibody fragments obtained by papain and pepsin digestion are Fab and F(ab')2 fragments respectively. In opsonization, IgG (IgA also) molecules bind to and coat antigenic particles and the bound IgG is recognized by IgG Fc receptors on leukocytes serving to enhance the efficiency of phagocytosis. (Abbas et al Cellular and Molecular Immunology. 1997,Third Edition. W.B. Saunders Company, Philadelphia, Chapter 3 pages 55-58). Several studies have been performed on the opsonizing power of IgG fragments derived after digestion with pepsin or papain. Shands et al (The Journal of Immunology 1966, 96:68-73) observed that the opsonizing activity of antibodies to *Salmonella typhimurium* was lost when Fab fragments were used. Kazmierowski et al (The Journal of Immunology, 1971 106:605-610) revealed that the opsonizing activity of gamma-globulin resided in the Fc region of the molecule and that removal or alteration of this region

resulted in a marked reduction in opsonic activity. Van Oss et al (G. J. Reticuloendothel. Soc.13:221) teaches that F(ab)2 or Fab fragments of pooled IgG to gram positive and gram negative organism exhibited no opsonizing activity. In contrast, another study by Perkins et al shows that F(ab')2 and Fab' fragments were able to enhance phagocytosis of Group A Streptococci. However, a later study by Fischetti et al (The Journal of Immunology, 1983, 130:896-902) showed that Fab' and F(ab'2) antibody fragments were unable to mediate phagocytosis of Group A Streptococci and explained that the results of Perkins et al may be partially explained by the presence of small quantities of undigested IgG in the preparations (See Fischetti et al p. 901 column 1 last bridging paragraph to column 2. Thus, it is highly unlikely that functional antibody fragments without the requisite Fc portion are able to promote phagocytosis by neutrophils. For, this reason more guidance and/or working example is needed to demonstrate that the instant desired functional antibody fragments without Fc portion have activity of promoting human neutrophilic phagocytosis of *P. gingivalis* bacteria). As to alteration of the amino acid sequence of a heavy chain constant region of the instant isolated antibody (see claim 17), said alterations include deletion of a heavy chain constant region of the Fc portion of the antibody which might affect binding to Fc receptors and thus affect the activity of promoting human neutrophilic phagocytosis. Also, the art teaches that heavy chain constant domains (CH) affect affinity and specificity of antigen, thus alterations of a heavy chain constant region can alter the specificity of the instant antibody (See review article by Torres et al. Trends in Immunology Vol. 29: 91-97, see entire document especially p. 93 column 1 last bridging column to column 2, p. 94 box 2., p. 95 column 1 second to the last paragraph to column 2). Thus, it is unpredictable that any alteration to a heavy chain constant region amino acid sequence will result

in an antibody that is able to bind to the same antigen or partake in binding to Fc receptors and thus have the activity of coaggregation of *P. gingivalis* and activity of promoting human neutrophilic phagocytosis and be able to suppress alveolar bone resorption due to *P. gingivalis*.

As to claim 49, the claim is drawn to a protein encoded by the nucleic acid possessed by a hybridoma selected from the group consisting of a hybridoma h13-17 (accession No. FERM BP-8325), a hybridoma 5-89-2 (accession No. FERM BP-8323), and a hybridoma a44-1 (accession No. FERM BP-8324) and encodes an antibody containing *a* variable region of an antibody produced by the hybridoma or a functional fragment of the antibody, which is an antibody or a functional fragment of the antibody.

The antigen binding site of an antibody is made up of three CDRs in the heavy chain variable region and three CDRs in the light chain variable region. See Abbas et al. Cellular and Molecular Immunology 4th edition, 1997 Chapter 3 p. 41-46. The three CDRs of the heavy chain variable region and the three CDRs of the light chain variable region are brought together in three dimensional space to form an antigen binding site.

The state of the art recognized that in general all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region were important for determining the ability of an antibody in any of a variety of forms (scFv, whole, etc.) to bind antigen. For example, Bendig et al (Methods: A Companion to Methods in Enzymology 1995; 8: 83-93) reviews that the general strategy for "humanizing" antibodies involves the substitution of all six CDRs from a rodent antibody that binds an antigen of interest, and that all six CDRs are involved in antigen binding (see entire document, but especially Figures 1-3). Similarly, the skilled artisan recognized a "chimeric" antibody to be an antibody in which both the heavy chain

variable region (which comprises the three heavy chain CDRs) and the light chain variable region (which comprises the three light chain CDRs) of a rodent antibody or the human CDRs with other human framework regions are recombined with constant region sequences from a human antibody of a desired isotype (see entire document, but especially Figures 1-3). The state of the art recognized that it would be highly unpredictable that a specific binding member comprising an antibody variable region but comprising less than all six CDRs of a parental antibody with a desired specificity would bind the same antigen as the parental antibody. Thus the minimal structure which the skilled artisan would consider predictive of the function of binding includes six CDRs i.e. from *both* heavy chain and light chain variable regions (three CDRS in the heavy chain variable region and three CDRs in the light chain variable region) from the same parental antibody in the context of an antibody framework.

Thus it would be highly unpredictable that the instantly recited antibody containing a variable region (i.e. a single variable region) thus comprising fewer than all six CDRs (i.e. three CDRs defined in the heavy chain variable region or three CDRs defined in the light chain variable region) of a particular reference antibody would have the same specificity as the reference antibody. Further, the antibody structure is not a random combination of heavy and light chain variable regions. The antibody paratope, binds an epitope on an antigen. The paratope of the antibody is highly specific and provides for a specific three-dimensional pocket in which the epitope of the antigen binds. The pocket is dependent on the specific primary structure of the complementary determining regions provided in a framework of other regions in a specific order. The specification does not describe nor enable an antibody or functional fragment of said antibody produced by the instant hybridomas that comprises a single variable

region. The specification does not provide any guidance as to antibodies to 40 kDa OMP of *P. gingivalis* produced by the instant hybridomas and comprises a single variable region or fragments of such antibodies. All both variable regions comprising the 3 CDRs of the heavy chain variable region and all 3 CDRs of the light chain variable region participate in antigen binding. It is unpredictable that an antibody that comprises just one variable region would recognize 40 kDa OMP of *P. gingivalis* and Applicants specification does not provide evidence to the contrary.

In view of the above, undue experimentation would be required of the skilled artisan to make and use the full scope of the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 is drawn to a protein encoded by the nucleic acid possessed by a hybridoma selected from the group consisting of a hybridoma h 13-17 (accession No. FERM BP-8325), a hybridoma 5-89-2 (accession No. FERM BP-8323), and a hybridoma a44-1 (accession No. FERM BP-8324) and encodes an antibody containing a variable region of an antibody produced

by the hybridoma or a functional fragment of the antibody, which is an antibody or a functional fragment of the antibody.

The claim is indefinite because it is not clear as written whether it is the nucleic acid that encodes an antibody containing a variable region of an antibody produced by the hybridoma or a functional fragment of the antibody or it is the hybridoma that encodes an antibody containing a variable region of an antibody produced by the hybridoma or a functional fragment of the antibody. Applicants are urged to clarify what is being claimed by rewording of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 6, 7, 14, 15, 54, and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al. J. Periodontol 1999; 70: 610-617.

The claims are drawn to an isolated antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Saito et al teaches a polyclonal antibody preparation comprising (r40-kDa antibody) binding to 40 kDa OMP (see abstract) wherein the antibody is the active ingredient. Said r40-

kDa antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* and has activity of promoting human neutrophilic phagocytosis (abstract and p. 610 first bridging paragraph to p. 611 column1). The r40-kDa antibody has the same activities and specificities as with the instant claims, therefore absent evidence to the contrary will also have activity of suppressing alveolar bone resorption. Saito et al teaches polyclonal r40-kDa thus said polyclonal include antibodies of many classes subclasses including class IgG and IgG1 which are able to bind via Fc portion to Fc receptors on neutrophils as evidenced by the demonstrated osponophagocytosis of *P. gingivalis* by human neutrophils (see abstract and p. 611 column 2 under preparation of r40-kDa antibody. The instant claims are drawn to the products i.e. the antibody and not intended uses for said products. Thus, Saito et al anticipates the agent set forth in claims 54 and 61, as set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2, 6, 7, 9, 10-15, 54, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 and Alakhov et al. US 5,840,319, 1998.

The claims are drawn to an isolated antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis wherein the antibody covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent.

Saito et al teaches a preparation comprising antibody binding to 40 kDa OMP as an active ingredient. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See abstract). Saito et al teaches monoclonal antibodies to 40 kDa outer membrane protein (OMP of *P. gingivalis*) of the IgG1 isotype produced by several hybridomas including Pg-ompA2 which inhibited coaggregation of *P. gingivalis* (see table 1) and the reference also teaches on p. 679 column 1 paragraph before the discussion section, that IgG1 from Pg-ompA2 hybridoma opsonizes bacteria and has a high complement activating capacity. Thus, the Pg-ompA2 IgG1 will promote human neutrophil phagocytosis (opsonophagocytosis). The antibodies have the same activity and absent evidence to the contrary will also have activity of suppressing alveolar bone resorption. Said antibody is produced by a mouse-mouse hybridoma (see p. 675 under monoclonal antibodies and hybridoma cells isolated from mice immunized with recombinant 40 kDa OMP); said antibody is a monoclonal antibody (p. 675 monoclonal antibodies). Saito et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 677 first paragraph under results). The instant claims are drawn to the products i.e. the

antibody and not to intended uses of said products. Thus, Saito et al anticipates the agent set forth in claims 54 and 61, as set forth above.

Saito et al does not teach that said antibody covalently bound to therapeutic agents such as antibiotics or antibacterial, for example tetracycline or minocycline.

Carroll et al teach antibody-antibiotic conjugates. Carroll et al teach that antibodies have many reactive groups that can be used in covalent conjugation to antibodies and teaches fragments of antibodies to make antibody-antibiotic conjugates (fig. 1B, column 11, and column 14 lines 59-64, column 15 lines 46-50. Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing (column 9 lines 15-23).

Alakhov teaches antibiotic or antibacterial therapeutic agents such as tetracycline or minocycline that are non-covalently bound to an antibody (column 2 lines 59-61, column 3 and 4 definition of chemotherapeutic agent and targeting moiety, column 12 lines 28-30 and lines 48-51 and column 15 lines 16-18).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to bind or link an antibiotic or antibacterial covalently to the antibody of Saito et al as taught by Carroll et al because Carroll et al teach antibodies and functional fragments have many reactive groups that can be used in covalent conjugation to antibodies and because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing.

Further, Alakhov teaches antibiotics/antibacterial such as tetracycline or minocycline that can be used to make such conjugates.

Claims 2, 6, 7, 8, 10-15, 54, and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 and Alakhov et al. US 5,840,319, 1998.

The claims are drawn to an isolated antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis wherein the antibody covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent.

Abiko et al teaches preparation comprising an antibody binding to 40 kDa OMP as an active ingredient. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See p. 3966 – abstract, right column which teaches that *Actinomyces viscosus* is now included in *Actinomyces naeslundii* and p. 3967 fig. 2). Said antibody is a human antibody; said antibody is a monoclonal antibody (see whole article). Abiko et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 3967 bottom of first incomplete paragraph). Abiko et al teaches IgG1 antibodies and thus said antibody binding to 40 kDa OMP will inherently have activity of promoting human neutrophilic phagocytosis since IgG antibodies have this capability; and will also have the activity of suppressing alveolar bone resorption. The instant claims are drawn to the products i.e. the antibody and not intended uses of said products. Thus, Abiko et al anticipates the agent set forth in claims 54 and 61 as set forth above.

Abiko et al does not teach that said antibody covalently bound to therapeutic agents such as antibiotics or antibacterial, for example tetracycline or minocycline.

Carroll et al teach antibody-antibiotic conjugates. Carroll et al teach that antibodies have many reactive groups that can be used in covalent conjugation to antibodies and teaches fragments of antibodies to make antibody-antibiotic conjugates (fig. 1B, column 11, and column 14 lines 59-64, column 15 lines 46-50. Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing (column 9 lines 15-23).

Alakhov teaches antibiotic or antibacterial therapeutic agents such as tetracycline or minocycline that are non-covalently bound to an antibody (column 2 lines 59-61, column 3 and 4 definition of chemotherapeutic agent and targeting moiety, column 12 lines 28-30 and lines 48-51 and column 15 lines 16-18).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to bind or link an antibiotic or antibacterial covalently to the antibody of Abiko et al as taught by Carroll et al because Carroll et al teach antibodies and functional fragments have many reactive groups that can be used in covalent conjugation to antibodies and because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing.

Claims 2, 6, 7, 11-15, 54, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. J. Periodontol 199; 70: 610-617 in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 and Alakhov et al. US 5,840,319, 1998.

The claims are drawn to an isolated antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic

phagocytosis wherein the antibody covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent.

Saito et al teaches an polyclonal antibody preparation (r40-kDa antibody) binding to 40 kDa OMP (see abstract) wherein the antibody is the active ingredient in the preparation. Said r40-kDa has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* and has activity of promoting human neutrophilic phagocytosis (abstract and p. 610 first bridging paragraph). The r40-kDa has the same activities and specificities as with the instant claims, therefore absent evidence to the contrary will also have activity of suppressing alveolar bone resorption. Saito et al teaches polyclonal r40-kDa thus said polyclonal include antibodies of many classes subclasses including class IgG and IgG1 which are able to bind via Fc portion to Fc receptors on neutrophils as evidenced by the demonstrated osponophagocytosis of *P. gingivalis* by human neutrophils (see abstract and p. 611 column 2 under preparation of r40-kDa antibody. The instant claims are drawn to the products i.e. the antibody and not intended uses of said products. Thus, Saito et al anticipates the agent set forth in claims 54 and 61, as set forth above.

Saito et al does not teach that said antibody covalently bound to therapeutic agents such as antibiotics or antibacterial, for example tetracycline or minocycline.

Carroll et al teach antibody-antibiotic conjugates. Carroll et al teach that antibodies have many reactive groups that can be used in covalent conjugation to antibodies and teaches fragments of antibodies to make antibody-antibiotic conjugates (fig. 1B, column 11, column 14 lines 59-64, column 15 lines 46-50. Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing (column 9 lines 15-23).

Alakhov teaches antibiotic or antibacterial therapeutic agents such as tetracycline or minocycline that are non-covalently bound to an antibody (column 2 lines 59-61, column 3 and 4 definition of chemotherapeutic agent and targeting moiety, column 12 lines 28-30 and lines 48-51 and column 15 lines 16-18).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to bind or link an antibiotic or antibacterial covalently to the antibody of Saito et al as taught by Carroll et al because Carroll et al teach antibodies and functional fragments have many reactive groups that can be used in covalent conjugation to antibodies and because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing.

Status of Claims

Claims 2, 6-47, 49, 54 and 61 are rejected. Claims 11, 20, 30, 40 and 67 are objected to. Claim 67 was not treated on the merits due to improper multiple dependency.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, either of the examiner's supervisors Shanon Foley (571-272-0898) or Robert Mondesi (571-272-0956) can be contacted.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645